

## REMARKS

Upon entry of the instant amendment claims 34 to 55 will be pending. Claims 35, 44, 48, 52 and 53 will have been amended. In addition, paragraph 0081 in the specification will have been amended. Applicants respectfully submit that no prohibited new matter has been introduced by the foregoing amendments.

The Office action dated February 10, 2006 has been carefully reviewed and the following reply is made in response thereto. In view to of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

### Summary of Office Action

1. Examiner has objected to claim 44 because it contains the trademark/trade name Novasomes.
2. Claims 52 and 53 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.
3. Claim 48 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description argument, allegedly because there is no support in the specification for a VLP in the range of 60 to 80 nm.
4. Claims 34-42 and 45-55 are rejected under 35 U.S.C. § 103(a) as unpatentable over Latham *et al.* and Saito *et al.*
5. Claims 34 and 43-45 are rejected under 35 U.S.C. § 103(a) as unpatentable over Latham *et al.* and Gupta *et al.*

### Amendment to the Specification and Claims 35 and 52

Applicants have amended paragraph 0081 to correctly refer to Figure 10 instead of Figure 8 in Example 13. Applicants point out that in the description of Figure 10 (paragraph 0031) it states that the figure depicts the neuraminidase activity of the avian influenza VLPs. Thus, Applicants assert that no new matter has been introduced.

Claim 35 was amended to correct the phrasing of the claim and claim 52 was amended to correct the spelling of hemagglutination.

**Claim Objections**

The Examiner has objected to claim 44 because it contains the trademark/trade name Novasome, thus rendering the claim indefinite.

In response, Applicants have amended claim 44 to remove the objected language and amended the claim to recite “non-ionic lipid vesicles.” Support for this amendment can be found in paragraph 0017. Thus in view of the claim amendment, Applicants request that the claim objection be reconsidered and withdrawn.

**Rejection under 35 U.S.C. § 112, Second Paragraph**

The Examiner has rejected claims 52 and 53 under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner alleges that the claims are drawn to levels of activity and recite a specific level, but there is no comparative basis or defined amount of initial substrate. Thus, the metes and bounds of the limitation cannot be determined without a relative comparative basis.

Applicant traverse this rejection. One of ordinary skill in the art would recognize the metes and bounds of the claims. However, in order to expedite prosecution, Applicants have amended claim 52 and 53 to recite “...when compared to a negative control.” Support for these amendments can be found in Examples 12 and 13 and Figures 9 and 10. Thus, in view of the claim amendments, Applicants request that this rejection be reconsidered and withdrawn.

**Rejection under 35 U.S.C. § 112, First Paragraph**

The Examiner has rejected claim 48 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Specifically, the Examiner asserts that a VLP range of 60-80 nm is not supported by the specification. However, the Examiner states that support for approximately 80 nm is supported.

In response, applicants have amended the claim to recite “...approximately 80 nm.” Thus in view of the claim amendments, Applicants request that this rejection be reconsidered and withdrawn.

**Rejections under 35 U.S.C. § 103**

The Examiner has rejected claims 34-42 and 45-55 under 35 U.S.C. § 103(a) as obvious under Latham *et al.* (J. of Virology 75, 6154-6165) in view of Saito *et al.* (Vaccine 20, 125-133). Specifically the Examiner asserts that Latham *et al.* discloses VLPs comprising HA, NA, M1 and M2 but does not teach avian influenza. Saito *et al.*, according to the Examiner, discloses H9N2, thus alleging that one of ordinary skill in the art would have been motivated to make H9N2 VLPs. In addition, Examiner also asserts that *in vitro* expressed HA and NA are well known to the art to have enzymatic activity (*i.e.* this is an inherent feature of the proteins).

Applicants traverse this rejection and assert that the Examiner has not met his burden of establishing a *prima facie* case of obviousness. “To establish *prima facie* obviousness of a claimed invention, all claim limitations must be taught or suggested by the prior art” (MPEP 2143.03). In the pending rejection, for instance, Applicants assert that none of the cited references disclose an influenza VLP, wherein the HA and/or the NA exhibit activity, let alone an avian VLP wherein the HA and/or NA exhibit activity. Although the Examiner asserts that *in vitro* expressed HA and NA are well known in the art to have enzymatic activity (Office Action at page 5), the Examiner has failed to provide a reference to support such an assertion. Applicants also respectfully point out that the HA and NA components on the claimed VLPs are not expressed *in vitro* but in a cell which transcribes and translates avian influenza HA and NA which are then expressed on the surface of said VLPs.

Also, Applicants respectfully refer the Examiner to § 2112 of the MPEP which states that “[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic.” The Federal Circuit has consistently upheld this doctrine. Further, it is well settled that consideration of an inherent quality is generally relevant only to anticipation, not obviousness. *Jones v. Hardy*, 220 USPQ 1021, 1025 (Fed. Cir. 1984).

For example in *In Re Rijckaert*, 9 F.3d 1531 (Fed. Cir. 1993), applicants were prosecuting claims directed toward a circuit that generated a time expansion or compression factor in recording systems. Specifically the claims comprised an algorithm that would generate a time expansion or compression according to three variables (number of recording head pairs, wrapping angle of the media and the relationship between signal time and recording time).

The claims in the application were rejected under 35 U.S.C. § 103 as being obvious over U.S. Patent 4,757,392 (Awamoto), in view of Driessen *et al.* (1986) “An Experimental Digital Video Recording System,” Transactions on Consumer Electronics, 362 to 370 (Driessen). Awamoto, the primary reference, disclosed a signal processing circuit for a video recording and reproducing apparatus. Specifically, Awamoto disclosed the use of one head pair with a specific wrapping angle. Driessen disclosed a recording system using two pairs of head mounted on specific actuators. The PTO asserted that when the “optimal” variables for time compression and expansion are plugged into the disclosed algorithm, the resulting configuration is the one disclosed in the Awamoto reference. Therefore the PTO asserted that Awamoto “inherently” disclosed the claimed invention. *Rijckaert*, 9 F.3d at 1533.

The Court stated that although inputting a certain set of variables in the disclosed algorithm may show the same configuration as disclosed in Awamoto, the use of these values are not inherent in Awamoto because the values of the variables cannot be presumed. *Rijckaert*, 9 F.3d at 1534. The Court stated that Awamoto never describes the use of time expansion and compression as a means of optimally filling track, much less suggest that the three variables are even a factor in compression. *Id.* Thus, it cannot be presumed that Awamoto considered these factors. The Court also concluded that it would be improper to retroactively determine that Awamoto’s device functions according to Rijckaert’s algorithm. *Id.* The Court stated that “[t]he mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish inherency (citations omitted). That which may be inherent is not necessarily known. Obviousness cannot be predicted on what is unknown (citations omitted).” *Id.*

In the instant case, the Examiner has asserted that the VLP HA and NA in the cited references are known in the art to have enzymatic activity. However, the Examiner has not pointed to any section in the cited references supporting this assertion nor has provided any supporting references. According to the Federal Circuit in *In Re Rijckaert*, an obviousness rejection cannot be predicted on what is unknown. Since the Examiner has not provided support for this assertion, the Examiner has not met his burden in establishing a *prima facie* case for obviousness.

Assuming, *arguendo*, that the Examiner can cite to a reference showing that HA and NA do have enzymatic activity when expressed, it cannot be presumed that the HA and NA in the

Latham *et al.* VLPs are active. To express a protein that exhibits activity, the protein must be folded in the correct conformation. Expression and folding is a complex process that may not yield proteins with activity, especially in an *in vivo* system. The references cited above, especially the Latham *et al.* reference, do not show nor suggest that the disclosed influenza HA or NA components in the VLP exhibit activity.

In another case, in *In Re Zurck*, 111 F.3d 887 (Fed. Cir. 1993), Applicants were prosecuting computer software claims that were directed toward a method for processing trusted commands. Specifically, the claims required that communication between a user and a trusted environment be along a “trusted path.”

The PTO rejected the claims under 35 U.S.C. § 103 based on two references. The primary reference was the UNIX operating system (UNIX) that discloses “trusted and untrusted environments.” The secondary reference, FILER version 2.0 (FILER2), discloses a repeat back mechanism to request that a potentially “dangerous” command be confirmed. The PTO stated that the only step not disclosed in these two references was the repeat back mechanism over the trusted environment. *In Re Zurck*, 111 F.3d at 888. The PTO argued that the repeat back mechanism over the trusted environment step is inherent in the art. They stated that “with regard to communication over a trusted path, if not explicit in the prior art, it is either inherent or implicit.” *Id.* The PTO also argued that because UNIX parses a command in an untrusted environment and executes it in a trusted environment that any confirmation communication must inherently be over a trusted pathway. They also stated that it is “basic knowledge that communication in trusted environments is performed over trusted paths.” *Id.*

The Court rejected the PTO’s argument. The Court stated that in rejecting the claim, the PTO relied on two references that did not explicitly or implicitly disclosed use of a trust path. The court stated that “[w]hile in retrospect...it might be logical to perform a repeat-back in the UNIX system over a trusted line, neither UNIX nor FILER2 teaches communicating with the user over a trusted pathway.” *In Re Zurck*, 111 F.3d at 889. Because neither UNIX or FILER2 teaches either explicitly or implicitly communicating with the user over a trusted pathway, the PTO clearly erred in its finding of inherency from the prior art.” *Id.* Thus, based on the record, the Court overturned the 35 U.S.C. § 103 rejection.

In the instant case, the Examiner has stated that “in vitro expressed HA and NA are well known in the art to have enzymatic activity” (Office Action at page 5). However, the Examiner has not pointed to any section in the cited references supporting this assertion nor has provided any supporting references in relation to the claimed activity in claim 34 or the embodiments of at least claims 52 and 53. As in *In Re Zurck*, since the rejection is not based on any factual findings, this obviousness rejection lacks substantial support and cannot stand because the Examiner has not met his burden of establishing a *prima facie* case of obviousness.

Therefore, in view of § 2112 of the MPEP, *In Re Rijckaert*, *In Re Zurck* and the above arguments, Applicants assert that the Examiner has not established a *prima facie* case of obviousness because the cited references do not teach nor suggest all the claim elements as required (see MPEP 2143.03). Specifically, the Examiner has not pointed to any section in the cited references nor has provided any supporting references showing that the HA and NA components in the Latham *et al.* VLPs have activity. Thus, Applicants request that this rejection under 35 U.S.C. § 103 be reconsidered and withdrawn.

The Examiner also asserts that the particle made by Latham *et al.* has the expected structure and immunoreactivity and it would be expected that the other VLPs would be similar and would also possess enzymatic activity (Office Action at page 4).

Applicants traverse this reasoning. Again, the Examiner does not cite to any references supporting this assertion. In addition, immunoreactivity does not necessarily relate to enzymatic activity. There are many examples in the art in which a protein has been used for immunizations in which said protein has been mutated or denatured to abolish its enzymatic activity (*e.g.* mutant toxins and toxoids). Also, just because the particles in Latham *et al.* look similar to the particle in the instant application does not necessarily mean that the NA or HA will exhibit activity. As stated above, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic (MPEP 2112). In view of the above arguments, Applicants request that this rejection be reconsidered and withdrawn.

The Examiner has rejected claims 34, and 43-45 under 35 U.S.C. § 103(a) as being unpatentable over Latham *et al.* and Gupta *et al.* (Vaccine 3, 219-225). Specifically the Examiner asserts that Latham *et al.* discloses VLPs and Gupta *et al.* discloses Novasomes, thus rendering the claims obvious.

Applicants traverse this rejection and assert that the Examiner has not met his burden of establishing a *prima facie* case of obviousness. "To establish *prima facie* case of obviousness of a claimed invention, all claim limitation must be taught or suggested by the prior art" (MPEP 2143.03). As stated above, Latham *et al.* does not disclose avian influenza HA or NA proteins expressed on a VLP. In addition, Latham *et al.* does not show nor suggest that the HA or NA exhibit activity. Gupta *et al.* does not disclose influenza vaccines in combination with adjuvants. Thus, the combined references do not teach or suggest all the claim elements. Therefore, the Examiner has not established a *prima facie* case of obviousness. In view of the above argument, Applicants request that this rejection be reconsidered and withdrawn.

### **Conclusion**

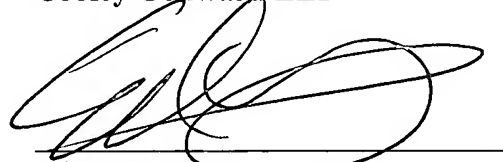
Applicant respectfully requests reconsideration of the subject application in view of the amendments to the claims and the above remarks. It is respectfully submitted that this application is now in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this amendment; the Examiner is requested to contact the Applicant's undersigned representative.

If there are any fees due in connection with the filing of this amendment, please charge the fees to our Deposit Account No. **50-1283**. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

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